REMARKS

The Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures required submission of a computer readable and paper copy of the sequence listing.

Applicants respectfully request acceptance of the enclosed paper copy and computer readable form of the Sequence Listing.

It is respectfully submitted that the amendments submitted herewith function only to insert the sequence listing to comply with 37 C.F.R. §1.821 to 1.825. These amendments are made without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

It is respectfully asserted that the sequence disclosure contained in the application now fully complies with the requirements set forth in 37 C.F.R. § 1.821 to § 1.825.

It is respectfully submitted that the Sequence Listing conforms to the requirements of 37 C.F.R. §1.823(b). The Statements required by 37 C.F.R §1.821(f) and (g) are set forth below.

Pursuant to 37 C.F.R. §1.821 (g), the undersigned hereby states that this submission, filed in accordance with 37 C.F.R. §1.821 (g), does not contain new matter.

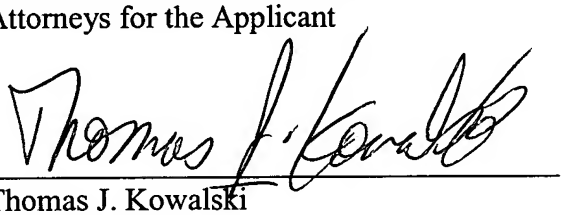
Pursuant to 37 C.F.R. §1.821 (f), the undersigned hereby states that the content of the paper and computer readable copies of the Sequence Listing submitted in accordance with 37 C.F.R. §1.821 (c) and (e), respectively, are the same.

CONCLUSION

In view of the amendments, remarks and enclosures herein, it is respectfully submitted that the application now complies with all requirements set forth in the Notice, including the requirements for computer readable disclosure of the biological sequences under 37 C.F.R. §1.821-1.825. Reconsideration and withdrawal of the Notice to Comply is earnestly solicited.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for the Applicant

By: 

Thomas J. Kowalski
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Tel. (212) 588-0800
Fax. (212) 588-0500

Enclosures: -Paper copy of Sequence Listing
-Computer Readable Copy of Sequence Listing
-Copy of Notice to Comply

REMARKS

The Notice to File Missing Parts required submission of an executed declaration, a surcharge for late filing of the declaration, and a computer readable and paper copy of the sequence listing.

Applicants respectfully request acceptance of the enclosed paper copy and computer readable form of the Sequence Listing and the declaration. In addition, a check in the amount of $65.00 is submitted herewith in payment of the required fee.

It is respectfully submitted that the amendments submitted herewith function only to insert the sequence listing and appropriate sequence identifiers into the text of the present application to comply with 37 C.F.R. §1.821 to 1.825. These amendments are made without prejudice, without admission, without surrender of subject matter, and without any intention of creating any estoppel as to equivalents.

It is respectfully asserted that the sequence disclosure contained in the application now fully complies with the requirements set forth in 37 C.F.R. § 1.821 to § 1.825.

It is respectfully submitted that the Sequence Listing conforms to the requirements of 37 C.F.R. §1.823(b). The Statements required by 37 C.F.R §1.821(f) and (g) are set forth below.

Pursuant to 37 C.F.R. §1.821 (g), the undersigned hereby states that this submission, filed in accordance with 37 C.F.R. §1.821 (g), does not contain new matter.

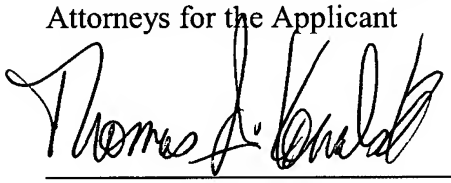
Pursuant to 37 C.F.R. §1.821 (f), the undersigned hereby states that the content of the paper and computer readable copies of the Sequence Listing submitted in accordance with 37 C.F.R. §1.821 (c) and (e), respectively, are the same.

CONCLUSION

In view of the amendments, remarks and enclosures herein, it is respectfully submitted that the application now complies with all requirements set forth in the Notice, including the requirements for computer readable disclosure of the biological sequences under 37 C.F.R. §1.821-1.825. Reconsideration and withdrawal of the Notice to File Missing Parts is earnestly solicited.

Respectfully submitted,

FROMMER LAWRENCE & HAUG LLP
Attorneys for the Applicant

By: 

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"VERSION WITH MARKINGS TO SHOW CHANGES MADE"

Page 27, line19:

Preferably, the nuclear receptor is one which interacts with its cognate response elements as a heterodimer with the retinoid X receptor (RXR). Thus, preferably, the nuclear receptor is one which forms a heterodimer, preferably with the retinoid X receptor, and is capable of recognising a response element in which two AGGTCA (SEQ ID NO: 23) binding sites are arranged in tandem. Preferably, binding and recognition is capable of causing modulation of gene expression of a gene linked to the response element. The response element may be in any control region of a gene, for example, in an upstream control region such as a promoter or enhancer. Target selection by the complexes requires the spacing between the binding sites to act as the identity element.

Page 30, line 15:

An example of a retinoic acid response element (RARE) is the sequence AGGTCA [5bp spacer] AGGTCA. (SEQ ID NO: 1) Another example of a retinoic acid response element is the DR-2 RARE with the sequence AGGTCA [2bp spacer] AGGTCA. (SEQ ID NO: 2)

Page 31, line 10:

Vitamin D Response Element

The consensus Vitamin D Response Element (VDRE) has the following sequence: GGGTGA NNG GGGGCA. (SEQ ID NO: 3) Another example of a vitamin D response element is the sequence AGGTCA [3bp spacer] AGGTCA. (SEQ ID NO: 4)

Page 32, line 22:

The Peroxisome Proliferator-Activated Receptor (PPAR) Response Element has a sequence AGGTCA [1bp spacer] AGGTCA (SEQ ID NO: 5), and is involved in regulation of expression of genes including cyclooxygenase (COX2), cytosolic phospholipase A2 (CPLA2), mitochondrial fatty acid beta–oxidising enzymes, ABCA1, ARE6, ARE7, GLUT2. Examples of disorders associated with abnormal, ectopic or over-expression of PPAR response element mediated genes include artherosclerosis, rheumatoid arthritis, inflammatory bowel disease, obesity, hypertension, diabetes, hyperlipidemia, colon cancer.

Page 33, line 5:

Thyroid Response Element

The thyroid response element has a consensus sequence 5'-AGGTCA [4bp spacer] AGGTCA -3' (SEQ ID NO: 6), and is involved in regulation of expression of a variety of genes, including connexin43, hyperpolarization-activated cyclic nucleotide-gated channel gene (HCN2), C/EBPalpha, prohormone convertases (PC1) and (PC2), Purkinje cell protein (Pcp-2), Calbindin, Myo-inositoltriphosphate (IP-3) receptor, Neurotrophin-3 (NT-3), Nerve growth factor (NGF), Brain-derived nerotrophic factor (BDNF), Neurotrophin 4/5, Reelin, Neural cell adhesion molecule (NCAM), Tenascin-C, Srg1, Hairless, BCL-2, Myelin basic protein (MBP), pro-alpha1(I) collagen, uncoupling protein 3 (UCP3), medullary thyrotropin-releasing hormone (TRH), beta-amyloid precursor protein (APP), fatty acid synthase promoter, malic enzyme, steroid receptor coactivator-1 (SRC-1), sodium, potassium-adenosine triphosphatase alpha3, apolipoprotein CII and lipocalin-type prostaglandin D synthase (beta-trace), among others.

Page 34, line 7:

Diseases which may be treated by the methods and compositions described here include those involving over-expression, ectopic expression, or abnormal expression for other response elements including COUP-TR (chicken ovalbumin upstream promoter transcription factor II). Diseases associated with such expression from COUP-TR include Type I mature onset diabetes of the young (MODY1); genes which are under the control of this response element include hepatocyte nuclear factor 1. The chicken ovalbumin upstream promoter transcription factor II response element has a sequence AGGTCA [1bp spacer] AGGTCA (SEQ ID NO: 7).

Page 80, line 10:

Example 1. Synthesis of Retinol Binding Protein Receptor Protein in Human Keratinocytes and Psoriatic Plaques

Anti-human retinol binding protein receptor peptide antibody is generated as follows. A cDNA corresponding to the retinol binding protein receptor expressed in humans (GenBank Accession Number NM_000329) is used as basis for the design of a 9 amino acid peptide. The peptide has the following sequence: VNGATAH[P]NH. (SEQ ID NO: 8)

Page 83, line 19:

Generation of Keratin 1 DNA Probe

A sequence of the human K1 cDNA (1046-1630 was amplified by PCR (*Pfu* Polymerase 35 cycles) using primers 5'-GCATCATTGCTGAGGTCAAGGC-3' (SEQ ID NO: 9) and 3'-CACCTCCAGAACCATAGC-5'. (SEQ ID NO: 10) This sequence was cloned into JM109 cells (Promega) using PCR-Script Amp Cloning Kit (Stratagene) and cells scaled up in LB Broth. The plasmid DNA was extracted from the JM109 cells using HiSpeed Plasmid Midi Kit (QIAGEN). The probe sequence was cut out using BamH1 and SacII restriction Enzymes (Promega). The DNA was run on a 1.5% Agarose gel, cut out and purified using QIAexII Gel Extraction Kit (QIAGEN).

Page 91, line 1:

Amino acids are numbered as in Cowan et al., *Proteins: Structure, Function and Genetics* 1990:8, p. 44-61. Peptides 589 (*Gly-Arg-Val-Arg-Leu-Leu-Asn-Asn-Trp-Asp-Val-Cys-Ala*) (SEQ ID NO: 11) and 592 (*Met-Lys-Tyr-Trp-Gly-Val-Ala-Ser-Phe-Leu-Gln-Lys-Gly-Asn-Asp*) (SEQ ID NO: 12) are synthesised to mimic the proposed binding regions of RBP to its receptor, by Arthur Moir, University of Sheffield.

Page 110, line 1:

Standard protocols for PCR are used to generate probes to analyze differentiation status. Probes are made against K1, K10 and CRABP II, using the following primer pairs:

K10

Primer sense 726-743	TGGAGGCTGACATCAACG (SEQ ID NO: 13)
Primer antisense 1257-1278	TATTCAGTATTCTGGCACTCGG (SEQ ID NO: 14)
Probe 726-1278 = 552 bp	
Primer sense 195-217	CAGGTGGCTATGGAGGATTAGG (SEQ ID NO: 15)
Primer antisense 687-708	ACCTCATTCTCATACTTCAGCC (SEQ ID NO: 16)
Probe 195-708 = 513 bp	

K1

Primer sense 1046-1067	GCATCATTGCTGAGGTCAAGGC (SEQ ID NO: 17)
Primer antisense 1613-1630	CACCTCCAGAACCATAGC (SEQ ID NO: 18)
Probe 1046-1630 = 584 bp	
Primer sense 422-441	GTGGTTATGGTCCTGTCTGC (SEQ ID NO: 19)
Primer antisense 1046-1067	GCCTTGACCTCAGCAATGATGC (SEQ ID NO: 20)
Probe 422-1067 = 645 bp	

CRABP II

Primer sense 214-235	ATGTGATGCTGAGGAAGATTGC (SEQ ID NO: 21)
Primer antisense 466-487	TCGTTGGTCAGTTCTCTGGTCC (SEQ ID NO: 22)
Probe 214-487 = 273 bp	